



<b>Title</b>	<b>DIRECTED DIFFERENTIATION AND MATURATION OF STEM CELL-DERIVED CARDIOMYOCYTES</b>
<b>Inventor(s)</b>	<b>LI, RONALD; FU, JI-DONG</b>
<b>Citation</b>	<b>WO Published patent application WO 2009152482. World Intellectual Property Organization (WIPO), PatentScope, 2009</b>
<b>Issued Date</b>	<b>2009</b>
<b>URL</b>	<b><a href="http://hdl.handle.net/10722/195293">http://hdl.handle.net/10722/195293</a></b>
<b>Rights</b>	<b>Creative Commons: Attribution 3.0 Hong Kong License for public patent documents</b>

(43) International Publication Date  
17 December 2009 (17.12.2009)(51) International Patent Classification:  
C12N 5/071 (2010.01)[CN/US]; c/o University of California, Davis, One  
Shields Avenue, Davis, CA 95616 (US).(21) International Application Number:  
PCT/US2009/047287(74) Agent: **KONSKI, Antoinette, F.**; Foley & Lardner LLP,  
975 Page Mill Road, Palo Alto, CA 94304-1013 (US).(22) International Filing Date:  
12 June 2009 (12.06.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
61/061,093 12 June 2008 (12.06.2008) US(71) Applicant (for all designated States except US): **THE  
REGENTS OF THE UNIVERSITY OF CALIFOR-  
NIA** [US/US]; 1111 Franklin Street, 12th Floor, Oakland,  
CA 94607-5200 (US).

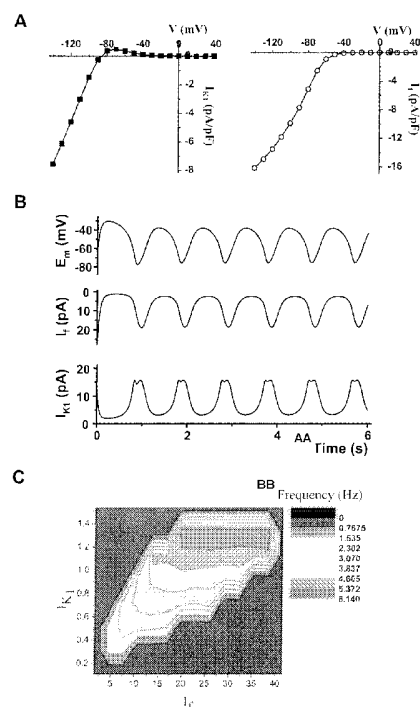
(72) Inventors; and

(75) Inventors/Applicants (for US only): **LI, Ronald**  
[CA/US]; c/o University Of California, Davis, One  
Shields Avenue, Davis, CA 95616 (US). **FU, Ji-Dong**(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,  
CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO,  
DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,  
HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,  
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,  
ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,  
NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD,  
SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT,  
TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ,  
TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,

[Continued on next page]

(54) Title: DIRECTED DIFFERENTIATION AND MATURATION OF STEM CELL-DERIVED CARDIOMYOCYTES

Figure 20

(57) Abstract: This invention provides an isolated electrophysiologically im-  
mature cell or its derivative that has been modified to provide a mature elec-  
trophysiological phenotype and populations of these cells. Compositions  
containing these cells and populations of cells are also provided by this in-  
vention. These cells and compositions have therapeutic and diagnostic uses.  
Non-limiting therapeutic uses include regenerating cardiac tissue, improving  
cardiac function, restoring action potential of cardiac tissue; and treating or  
preventing cardiac malfunction. The cells and population of cells also can be  
used diagnostically to screen drug or other therapeutic candidate.



MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR),  
OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments (Rule 48.2(h))*

**Published:**

— *with international search report (Art. 21(3))*

**(88) Date of publication of the international search report:**

22 April 2010

## INTERNATIONAL SEARCH REPORT

International application No.  
**PCT/US2009/047287****A. CLASSIFICATION OF SUBJECT MATTER***C12N 5/071(2010.01)i*

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC C12N, A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

KOMPASS (KIPO internal) &amp; PubMed (key words: cardiac cell, pacemaker, differentiatiaon)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	SARTIANI, L. et al., 'Developmental Changes in Cardiomyocytes Differentiated from Human Embryonic Stem Cells: A Molecular and Electrophysiological Approach.' Stem Cells, 2007, Vol. 25, pp.1136-1144. See abstract and figures 2-7	1 - 3 11,12
X Y	TOMITA, Y. et al., 'Application of mesenchymal stem cell-derived cardiomyocytes as bio-pacemakers:current status and problems to be solved.' Med. Bio. Eng. Comput., 30 Jan. 2007, Vol. 45, pp.209-220.	1 - 3 11,12
Y	TSE, H.-F. et al., 'Bioartificial Sinus Node Constructed via In Vivo Gene Transfer of an Engineered Pacemaker HCN Channel Reduces the Dependence on Electronic Pacemaker in a Sick-Sinus Syndrome Model.' Circulation, 21 Aug. 2006, Vol. 114, pp.1000-1011.	11,12
Y	US 2004/0254134 A1 (MARBAN, E & Li, R.) 16 Dec. 2004	11,12



Further documents are listed in the continuation of Box C.



See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&amp;" document member of the same patent family

Date of the actual completion of the international search

08 MARCH 2010 (08.03.2010)

Date of mailing of the international search report

**09 MARCH 2010 (09.03.2010)**

Name and mailing address of the ISA/KR

Korean Intellectual Property Office  
Government Complex-Daejeon, 139 Seonsa-ro, Seo-  
gu, Daejeon 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

KIM, KYOUNG MI

Telephone No. 82-42-481-8161



**INTERNATIONAL SEARCH REPORT**

International application No.

**PCT/US2009/047287****Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 4-10, 13-15  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No.

**PCT/US2009/047287**

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004-0254134 A1	16.12.2004	AU 2002-338529 A1	11.11.2002
		AU 2002-338529 A8	11.11.2002
		CA 2445578 A1	07.11.2002
		EP 1409510 A4	08.09.2004
		EP 1409510 A2	21.04.2004
		JP 1653-4015nu I I	11.11.2004
		JP 2009-148572 A	09.07.2009
		JP 2004-534015 A	11.11.2004
		WO 2002-087419 A2	07.11.2002
		WO 2002-087419 A3	07.11.2002